Inducible Expression of GDNF in Transplanted iPSC-Derived Neural Progenitor Cells.

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Public Summary:
Trophic factor delivery to the brain using stem cell-derived neural progenitors is a powerful way to bypass the blood-brain barrier. Protection of diseased neurons using this technology is a promising therapy for neurodegenerative diseases. Glial cell line-derived neurotrophic factor (GDNF) has provided benefits to Parkinsonian patients and is being used in a clinical trial for amyotrophic lateral sclerosis. However, chronic trophic factor delivery prohibits dose adjustment or cessation if side effects develop. To address this, we engineered a doxycycline-regulated vector, allowing inducible and reversible expression of a therapeutic molecule. Human induced pluripotent stem cell (iPSC)-derived neural progenitors were stably transfected with the vector and transplanted into the adult mouse brain. Doxycycline can penetrate the graft, with addition and withdrawal providing inducible and reversible GDNF expression in vivo, over multiple cycles. Our findings provide proof of concept for combining gene and stem cell therapy for effective modulation of ectopic protein expression in transplanted cells.

Scientific Abstract:
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